

Claims

1. A method for displaying a (poly)peptide/protein on the surface of a bacteriophage particle comprising:
causing or allowing the attachment of said (poly)peptide/protein after expression to a member of the protein coat of said bacteriophage particle, wherein said attachment is caused by the formation of a disulfide bond between a first cysteine residue comprised in said (poly)peptide/protein and a second cysteine residue comprised in said member of the protein coat.
2. The method of claim 1, wherein said second cysteine residue is present at a corresponding amino acid position in a wild type coat protein of a bacteriophage.
3. The method of claim 2, wherein said member of the protein coat is a wild type coat protein of a bacteriophage.
4. The method of claim 2, wherein said member of the protein coat is a truncated variant of a wild type coat protein of a bacteriophage, wherein said truncated variant comprises at least that part of said wild type coat protein causing the incorporation of said coat protein into the protein coat of the bacteriophage particle.
5. The method of claim 2, wherein said member of the protein coat is a modified variant of a wild type coat protein of a bacteriophage, wherein said modified variant is capable of being incorporated into the protein coat of the bacteriophage particle.
6. The method of claim 1, wherein said second cysteine residue is not present at a corresponding amino acid position in a wild type coat protein of a bacteriophage.
7. The method of claim 6, wherein said second cysteine has been artificially introduced into a wild type coat protein of a bacteriophage.
8. The method of claim 6, wherein said second cysteine has been artificially introduced into a truncated variant of a wild type coat protein of a bacteriophage.

9. The method of claim 6, wherein said second cysteine has been artificially introduced into a modified variant of a wild type coat protein of a bacteriophage.
10. The method of any one of claims 4 to 9, wherein said second cysteine is present at, or in the vicinity of, the C- or the N-terminus of said member of the phage coat of said bacteriophage particle.
11. The method of any one of claims 1 to 10, wherein said bacteriophage is a filamentous bacteriophage.
12. The method of claim 11, wherein said member of the protein coat of the bacteriophage particle is or is derived from the wild type coat protein pIII.
13. The method of claim 11, wherein said member of the protein coat of the bacteriophage particle is or is derived from the wild type coat protein pIX.
14. The method of any one of claims 1 to 12, comprising:
 - (a) providing a host cell harbouring a nucleic acid sequence comprising a nucleic acid sequence encoding said (poly)peptide/protein;
 - (b) causing or allowing the expression of said nucleic acid sequence; and
 - (c) causing or allowing the production of bacteriophage particles in said host cell.
15. The method of any one of claims 1 to 14, wherein said (poly)peptide/protein comprises an immunoglobulin or a functional fragment thereof.
16. The method of claim 15, wherein said functional fragment is an scFv or Fab fragment.
17. A nucleic acid sequence encoding a modified variant of a wild type coat protein of a bacteriophage, wherein said modified variant consists of:
 - (a) one or more parts of said wild type coat protein of a bacteriophage, wherein one of said parts comprises at least that part which causes or allows the incorporation of said coat protein into the phage coat; and

- (b) between one and six additional amino acid residues not present at the corresponding amino acid positions in a wild type coat protein of a bacteriophage, wherein one of said additional amino acid residues is a cysteine residue.
18. A nucleic acid sequence encoding a modified variant of a wild type coat protein of a bacteriophage, wherein said modified variant consists of
- (a) one or more parts of said wild type coat protein of a bacteriophage, wherein one of said parts comprises at least that part which causes or allows the incorporation of said coat protein into the phage coat;
 - (b) between one and six additional amino acid residues not present at the corresponding amino acid positions in a wild type coat protein of a bacteriophage, wherein one of said additional amino acid residues is a cysteine residue; and
 - (c) one or more peptide sequences for purification and/or detection purposes.
19. A vector comprising the nucleic acid of claim 17 or 18.
20. The vector of claim 19, further comprising one or more nucleic acid sequences encoding a (poly)peptide/protein comprising a second cysteine residue.
21. The vector of claim 20, wherein said (poly)peptide/protein comprises an immunoglobulin or a functional fragment thereof.
22. A host cell comprising the nucleic acid sequence of claim 17 or 18, the vector of any one of claims 19 to 21.
23. A modified variant of a wild type coat protein of a bacteriophage encoded by the nucleic acid sequence of claim 17 or 18, the vector of any one of claims 19 to 21, or produced by the host cell of claim 22.
24. A bacteriophage particle displaying a (poly)peptide/protein on its surface obtainable by a method comprising:

causing or allowing the attachment of said (poly)peptide/protein after expression to a member of the protein coat of said bacteriophage particle, wherein said attachment is caused by the formation of a disulfide bond between a first cysteine residue comprised in said (poly)peptide/protein and a second cysteine residue comprised in said member of the protein coat.

25. A bacteriophage particle displaying a (poly)peptide/protein attached to its surface, wherein said attachment is caused by the formation of a disulfide bond between a first cysteine residue comprised in said (poly)peptide/protein and a second cysteine residue comprised in a member of the protein coat of said bacteriophage particle.
26. The bacteriophage particle of claim 24 or 25, further comprising a vector comprising one or more nucleic acid sequences encoding said (poly)peptide/protein.
27. The bacteriophage particle of claim 26, wherein said vector is the vector of claim 20 or 21.
28. A diverse collection of bacteriophage particles of any one of claims 25 to 27, wherein each of said bacteriophage particles displays a (poly)peptide/protein out of a diverse collection of (poly)peptides/proteins.
29. A method for obtaining a (poly)peptide/protein having a desired property, comprising:
 - (a) providing the diverse collection of bacteriophage particles of claim 28; and
 - (b) screening said diverse collection and/or selecting from said diverse collection to obtain at least one bacteriophage particle displaying a (poly)peptide/protein having said desired property.
30. The method of claim 29, wherein said desired property is binding to a target of interest.
31. The method of claim 30, wherein step (b) further comprises:
 - (ba) contacting said diverse collection of bacteriophage particles with the target of interest;
 - (bb) eluting bacteriophage particles not binding to the target of interest;

(bc) eluting bacteriophage particles binding to the target of interest by treating the complexes of target of interest and bacteriophages binding to said target of interest formed in step (ba) under reducing conditions.